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10/601,953

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Steven C. Quay

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11/28/2006

NASTECH PHARMACEUTICAL COMPANY INC
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EXAMINER

KOSAR, ANDREW D

ART UNIT

PAPER NUMBER

1654

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/601,953

Applicant(s)

QUAY, STEVEN C.

Examiner

Andrew D. Kosar

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-92 is/are pending in the application.
- 4a) Of the above claim(s) 6-9, 18-29, 48-81, 85, 86, 88 and 90 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 June 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. <u>20061120</u> . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/23/05</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

In view of the interview on November 20, 2006 with Applicant's representative, Peter Knudsen, the restriction requirement has been clarified as outlined below.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-47 and 82-92, drawn to permeabilizing peptides for enhancing mucosal epithelial paracellular transport and a pharmaceutical composition thereof, classified in class 514, subclass 2.
- II. Claims 48-81, drawn to a method of treating or preventing a disease or condition with the pharmaceutical composition of group I, classified in class 514, subclass 2.

The inventions are independent or distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the method is a general method of treating or preventing any disease, and thus one could practice the method with any compound, e.g. treating diabetes with insulin.

The search for each of the above inventions is not co-extensive particularly with regard to the non-patented literature search. A reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

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Additionally, the compounds of the instant application are distinct, absent evidence to the contrary, and would require a unique search strategy. The search for the distinct compounds is conducted based on their chemical structure. Therefore, the search of one chemical structure would not necessarily lead to the discovery of another structure, nor would it necessarily lead to the discovery of methods of using and/or making.

Because these inventions are independent or distinct for the reasons given above, the inventions require a different field of search (see MPEP § 808.02) and the search for one invention would not necessarily lead to the discovery of another invention, restriction for examination purposes as indicated is proper, and to not restrict would be an undue burden on the Examiner.

This application contains claims directed to a plurality of patentably distinct species: SEQ ID NOs: 4-10, 32-35, 42 and 54-63. The species are independent or distinct because each is structurally distinct and would be expected to function differently, particularly *in vivo*.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-9, 12-48, 50, 52-63, 65-90 and 92 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an

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allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

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During a telephone conversation with Applicant's representative, Peter J. Knudsen, on November 20, 2006, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-47 and 82-92, and the species SEQ ID NO:4. SEQ ID NO:4 has been determined to read upon claims 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6-9, 18-29, 48-81, 85, 86, 88 and 90 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92 have been examined on the merits.

During the course of examination, the examiner identified an additional species, not readable upon the elected species (VRIP), but readable upon the broader generic claims, and has included in the rejections below.

Specification

The disclosure is objected to because of the following informalities:

The use of the trademark(s), e.g., REFIB and AVONEX (table 14), has/have been noted in this application. A trademark should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Further, language such as "the product X (a descriptive name) commonly known as Y (trademark)" is impermissible, since such language does not bring out the fact that the latter is a

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trademark. Language such as “the product X (a descriptive name) sold under the trademark Y” is permissible. See MPEP § 608.01 (v).

Appropriate correction is required.

Please note, the lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims read upon naturally occurring peptides, including JAM-1, and the limitations of dependent claims do not *per se* limit the peptide in length, and thus also read on naturally occurring JAM-1, for example.

Claim Objections

Claims 10, 15, 17, 32 and 91 are objected to because of the following informalities:

In claim 15, FSF is not the abbreviation for follicle stimulating hormone and Chymotrypsin is misspelled chemotrypsin.

In claims 17 and 32, the roman numeral designations are not consistent with conventional practice and many are repeated.

While it is understood that in claims 10 and 91, the peptides recited are JAM, claudin and occludin fragments, the recitation of ‘JAM-1’, ‘occludin’, etc. is unnecessary and could be interpreted as being alternatives to the peptides. Alternatively, Applicant could place a colon

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between the text and the sequence, e.g. JAM-1 peptide: VRIP..., and separate the elements JAM-1, claudin, occludin by a new line.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.” *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include “level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of

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such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

“A written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) (“In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...”) *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4)

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functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the (5) method of making the claimed invention.

While all of the factors have been considered, a sufficient amount for a *prima facie* case are presented.

In the instant case, the claims are drawn to a myriad of peptides and compositions comprising proteins or fragments of proteins or analogs by substitution/deletion/insertion of the protein or fragment, where the protein is a JAM, occludin or claudin. The composition must further comprise a biological active agent and additional delivery enhancing agents.

(1) Level of skill and knowledge in the art:

Peptide fragments are known in the art, and the art recognizes JAM, occludin and claudin peptides. The art generally recognizes drugs and the classes, as well as the general classes of pH control agent, vasodilator, etc. which are the enhancing agents. However, the level of skill and knowledge in the art is low with regards to the myriad of combinations and the *a priori* knowledge that the virtually limitless number of combinations would function as claimed.

(2) Partial structure:

The claims provide structures for various elements, however no single claim fully defines one composition. The specification provides various peptide fragments with the asserted activity and provides several closely related compositions in the examples. However, most claims do not provide structure, but rather rely on the function, e.g. permeabilizing peptide, a ciliostatic agent, a vasodilatory agent, etc.

(3) Physical and/or chemical properties and (4) Functional characteristics:

The peptidic element must function as a permeabilizing peptide, however no specific structural element is coupled to the function. The additional elements, e.g. ciliostatic agent,

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vasodilatory agent, must also function as mucosal delivery-enhancing agent, which is generally a function not attributed to such compounds.

(5) Method of making the claimed invention:

Methods of making compositions are known in the art, however the methods of making the myriad of compositions as claimed and having the requisite activity are beyond those known in the art.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that the claims are broad generics with respect to all possible peptides, fragments and compositions encompassed by the claims. The possible variations in the structure of the peptide and the elements in the composition are limitless. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide a sufficient number of species of peptide with the requisite activity or compositions thereof. While having written description of the peptides shown to have the requisite activity and the compositions identified in the specification tables

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and/or examples, the specification is void of a sufficient number of species to show applicant was in possession of the genus of peptide and composition as instantly claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does “little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.”) Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claims 44 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, “Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is ‘undue’, not ‘experimentation’” (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. “Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations” (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

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(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a composition for treating female sexual dysfunction which is a subset of male dysfunction, as instantly claimed.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Female sexual dysfunction is not a subset of male sexual dysfunction, and thus it is highly unpredictable to formulate such a composition.

(5) The relative skill of those in the art:

The relative skill of those in the art is low with regards to such formulations.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance on making a limited number of compositions, however, the specification does not provide guidance on how one would make such a composition, particularly with compounds that are not recognized in the art as being used for treating female sexual dysfunction, e.g. EPO, HGH, natriuretic peptide.

(8) The quantity of experimentation necessary:

Considering that female dysfunction is not a subset of male dysfunction and the lack of guidance provided in the specification, one of ordinary skill in the art would be unduly burdened with making a pharmaceutical composition that is for treating female dysfunction as instantly claimed with out undue experimentation.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 10-17, 30-47, 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and 82 are vague and indefinite because they recite, "...inhibits/inhibiting homotypic binding of an epithelial membrane adhesive protein selected from a [JAM], occludin or claudin." It is unclear whether this recitation defines the peptide being claimed, or the protein interaction being inhibited, i.e. is the permeabilizing peptide being claimed selected from JAM, occludin or claudin- defining a starting point structure, or is the permeabilizing peptide being claimed a peptide that inhibits JAM, occludin or claudin- a peptide having no structure, and thus the claims are indefinite.

Claims 4, 5 and 82-84 recite, 'corresponding reference sequence' which is vague and indefinite, because the claims and specification do not define the reference sequence nor do the claims set forth the starting point from which comparisons are made, and one would not know what is, or is not, a corresponding sequence. For example, is murine JAM-1 a corresponding reference sequence human JAM-1 or -2?

Claim 15 lacks clear antecedent basis. Claim 15 includes compounds which are not therapeutic peptides or proteins, *per se*, and thus the claim lacks clear antecedent basis, and further, it is unclear how Applicant is intending to define a peptide or protein as many of the recited compounds are not peptides or proteins, e.g. estrogen, testosterone, ciclopirox, midazolam, opioids, etc.

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Claim 44 lacks clear antecedent basis. Female dysfunction is not a subset of male dysfunction, and thus lacks clear antecedent basis.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. 102(b) as being anticipated by LIU (Y. Liu, et al. J. Cell. Sci. (2000) 113, pages 2363-2374).

The instant claims are drawn generally to JAM-1 peptides, and in view of the elected species, the claims are drawn to peptides comprising VRIP

Liu teaches human JAM-1 (figure 1b, page 2366) which comprises the sequence VRIP and comprises from about 4-25 contiguous residues of the extracellular domain of JAM-1. Because the ‘reference sequence’ has not been defined, the teaching of huJAM-1 is considered to be a substitution/insertion/deletion variant of murine JAM-1. Further, please note, ‘between about’ does not set forth the limits on the number of residues in the peptide, and thus a teaching of the full length peptide, i.e.- human JAM-1, reads on the claims.

Claims 82-84, 91 and 92 are rejected under 35 U.S.C. 102(b) as being anticipated by BLASZCZYK-THURIN (WO 00/27420 A1).

Blaszczuk-Thurin teaches SEQ ID NO:119 (GLDLLGDVRIPVRR) (Table 1), which is a 15 amino acid sequence which comprises VRIP. SEQ ID NO:119 is interpreted as a peptide which comprises about 4 contiguous residues of JAM-1 with one or more addition/substitution/deletion of JAM-1.

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Claims 1-5, 12-14, 16, 17, 32-41 and 82-84 are rejected under 35 U.S.C. 102(a) as being anticipated by BLASCHUK (US Patent 6,391,855).

Blaschuk teaches a JAM peptide comprising JAM CAR sequence SFTIDPKSG (SEQ ID NO:2) (claim 1) in a pharmaceutical composition with a pharmaceutically acceptable carrier (claim 9) and a drug (claim 10). In looking to the specification, Blaschuk teaches that, "virtually any drug may be administered in combination with a modulating agent as described herein" (column 23, lines 51-52) and provides a myriad of drugs that can be used, including taxol, mitomycin C, indomethacin and ibuprofen, as well as generic antifungals, analgesics, vasodilators, narcotic antagonists (e.g. column 23, line 53 to column 24, line 6). The peptide of Blaschuk is an extracellular domain of murine JAM.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 are rejected under 35 U.S.C. 103(a) as being obvious over LIU, as applied to claims 82-84, 87, 89, 91 and 92, *supra*, in view of QUAY (US 2004/0028613 A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by:

(1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another";

(2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131;

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(3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c); or

(4) a showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The teachings of Liu are presented *supra*.

Quay teaches pharmaceutical compositions comprising dopamine receptor antagonist and one or more delivery enhancing agents formulated for nasal mucosal delivery (e.g. claim 2), where the dopamine receptor antagonist is apomorphine (claim 3). The composition of Quay overlaps with the instantly claimed compositions, as, for example, the elements of the composition of claim 5 of Quay overlaps with the elements of the composition of instant claim 32, including the vasodilatory agent, the mucolytic or mucus clearing agent, the ciliostatic agent and the modulatory agent of epithelial junction physiology. Quay teaches that the composition is used to treat male or female sexual dysfunction (e.g. claims 24 and 25) or erectile dysfunction (claim 23). Quay teaches that the composition can be formulated as a powder (e.g. paragraphs [0455], [0456] and [0473]) or as a nasal spray (e.g. paragraphs [0453], [0454] and [0473]).

The difference between Quay and the instant claims is that while Quay teaches the composition and provides that the composition can comprise a modulatory agent of epithelial junction physiology, Quay does not specifically teach JAM-1.

It would have been obvious at the time of the invention to have used JAM-1 peptide in the composition of Quay, as Quay teaches any modulatory agent of epithelial junction physiology, and JAM-1 of Liu is one such modulatory agent of epithelial junction physiology.

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One would have been motivated to have used any modulatory agent of epithelial junction physiology, including JAM-1, because Quay teaches that any modulatory agent of epithelial junction physiology can be used in the composition.

One would have had a reasonable expectation for success in making the composition with any modulatory agent of epithelial junction physiology, including JAM-1, as Quay teaches that any modulatory agent of epithelial junction physiology can be used in the claimed composition and because combining two elements in the formulation of a composition is a technique widely practiced in the medicinal arts.

With regards to the functional limitations, because the structural limitations of the composition are met, the composition must intrinsically possess the asserted activity.

Furthermore, the composition of Quay provides for the same claimed biological activities, e.g. Claim 14 provides peak concentration in CNS tissue that is 40% or greater compared to blood plasma, which corresponds to instant claim 41.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 1-5, 12-17, 32-44, 47 and 82-84 are rejected under 35 U.S.C. 103(a) as being obvious over Blaschuk, as applied to claims 1-5, 12-14, 16, 17, 32-41 and 82-84, *supra*, in view of PLATZ (US Patent 5,345,562).

The teachings of Blaschuk are presented *supra*.

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Platz teaches micronized polypeptide drug formulations as powders suitable for aerosol administration (e.g. column 2, lines 13-16). Platz teaches EPO, HGH, TPA, PDGF, TGF- β _{1,2} and 3, TGF- α , IGF-1 and 2, MGCSF, insulin, interleukin 1-7, interferon- α and - β (column 2, lines 31-32).

The difference between Blaschuk and the instant claims, is that while Blaschuk teaches the composition can have any drug or therapeutic agent, it does not teach the peptide.

It would have been obvious to have formulated the composition of Blaschuk with the peptides of Platz, as Blaschuk teaches any drug can be formulated in the composition.

One would have been motivated to have selected any peptide or protein, including the peptide drugs of Platz, because Blaschuk teaches the any drug can be formulated in the composition, and to increase the transcellular transport of the drugs of Platz.

One would have had a reasonable expectation for success in making the formulation, as Blaschuk teaches the composition can be formulated with any drug, and because combining elements in a formulation is a technique widely practiced in the medicinal arts.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection

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is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-58 of copending Application No. 09/891,630 (QUAY) in view of LIU.

The teachings of Quay and Liu are presented *supra*.

The difference between Quay and the instant claims is that while Quay teaches the composition and provides that the composition can comprise a modulatory agent of epithelial junction physiology, Quay does not specifically teach JAM-1.

It would have been obvious at the time of the invention to have used JAM-1 peptide in the composition of Quay, as Quay teaches any modulatory agent of epithelial junction physiology, and JAM-1 of Liu is one such modulatory agent of epithelial junction physiology.

One would have been motivated to have used any modulatory agent of epithelial junction physiology, including JAM-1, because Quay teaches that any modulatory agent of epithelial junction physiology can be used in the composition.

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One would have had a reasonable expectation for success in making the composition with any modulatory agent of epithelial junction physiology, including JAM-1, as Quay teaches that any modulatory agent of epithelial junction physiology can be used in the claimed composition and because combining two elements in the formulation of a composition is a technique widely practiced in the medicinal arts.

With regards to the functional limitations, because the structural limitations of the composition are met, the composition must intrinsically possess the asserted activity.

Furthermore, the composition of Quay provides for the same claimed biological activities, e.g. Claim 14 provides peak concentration in CNS tissue that is 40% or greater compared to blood plasma, which corresponds to instant claim 41.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

This is a provisional obviousness-type double patenting rejection.

Claims 1-5, 10-14, 16, 17, 30-44, 47, 82-84, 87, 89, 91 and 92 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-62 of copending Application No. 10/840,536 (QUAY(2), US 2004/02586663 A1; amended claim set of 8/15/06).

Quay(2) teaches compositions which are of an overlapping, if not commensurate scope, where the composition is interferon- α with one or more mucosal delivery agents, formulated for

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nasal delivery as a powder or spray (claims 2-3), comprising mucosal delivery-enhancing agents which overlap with the instant composition (e.g. claim 19), where the mucosal delivery-enhancing agent is a JAM protein (claim 33). In looking to the specification for JAM proteins which provide support for the claims, Quay(2) specifically identifies the peptides of the instant application as JAM peptides (e.g. paragraphs [0199] and [0200]).

This is a provisional obviousness-type double patenting rejection.

Claims 1-5, 10-14, 16, 17, 30-44, 47, 82-84, 87, 89, 91 and 92 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-50 and 53-57 of copending Application No. 10/462,452 (Quay(3), US 2004/0037809 A1; amended claim set of 10/10/06).

Quay(3) teaches compositions which are of an overlapping, if not commensurate scope, where the composition is interferon- β formulated for mucosal delivery with mucosal delivery-enhancing agents, e.g. aggregation inhibitory agent, ciliostatic agent, mucolytic agent or modulatory agent of epithelial junction physiology (e.g. claim 17). In looking to the specification for modulatory agent of epithelial junction physiology which provide support for the claims, Quay(3) provides a list of peptides, including JAM-1 and more specifically VRIP (paragraph [0247]).

This is a provisional obviousness-type double patenting rejection.

Claims 1-5, 10-13, 17, 30-46, 82-84, 87, 89, 91 and 92 are directed to an invention not patentably distinct from claims 1-58 of commonly assigned 09/891,630, for the reasons set forth *supra*.

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Claims 1-5, 10-14, 16, 17, 30-44, 47, 82-84, 87, 89, 91 and 92 are directed to an invention not patentably distinct from claims 1-62 of commonly assigned 10/840,536, for the reasons set forth *supra*.

Claims 1-5, 10-14, 16, 17, 30-44, 47, 82-84, 87, 89, 91 and 92 are directed to an invention not patentably distinct from claims 1-50 and 53-57 of commonly assigned 10/462,452, for the reasons set forth *supra*.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 09/891,630, 10/840,536 and 10/462,452, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

The examiner has identified three copending Applications which have been rejected under Double Patenting above. Because of Applicant's prolific Patent and Application portfolio, the burden is shifted to Applicant to identify all relevant Applications and Patents and to include said Applications and Patents on any terminal disclaimer filed.

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Conclusion

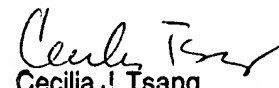
The prior art made of record as cited on the enclosed PTO-892 and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


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